ORIGINAL ARTICLE

OUTCOME OF ACUTE RENAL FAILURE IN CHILDREN WITH DIABETIC KETO ACIDOSIS (DKA)

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Abstract

The presentation and outcome of acute renal failure in children with diabetic ketoacidosis (DKA) were analyzed. Of the 130 DKA episodes treated at the Pediatric Intensive Care Unit (PICU), 15 children (11.5%) had renal failure. Sepsis and shock were the common etiological factors. Mortality in ARF complicating DKA was 40%. Persistent acidosis requiring bicarbonate therapy, reduction in intravenous fluid volume, reduced dose of insulin and peritoneal dialysis were the modifications in the treatment for this life threatening complication.

Keywords: Acute Renal failure, DKA, infections, shock

Introduction

Cerebral edema is a life threatening complication of diabetic ketoacidosis (DKA), other complications include dyselectrolytemia, acute respiratory distress syndrome (ARDS), pulmonary edema and renal failure. Chronic renal failure due to diabetic nephropathy and its presentation with DKA is encountered in adults. But children with new onset diabetes mellitus (DM) or known diabetic children presenting with acute renal failure (ARF) are rare. Literature reveals few case reports of DKA with renal failure. (1,2,3) Reported mortality in ARF complicating DKA is about 50%. (1) We are presenting a series of children with DKA and renal failure.

Methods and Materials

This retrospective study was undertaken to evaluate the outcome of children with ARF in DKA from January 2006 to August 2010 in 130 children who presented with DKA. None were known to have pre-existing renal disease. Children with raised blood urea and creatinine at presentation but normalized within few hours of fluid therapy were excluded. Study parameters included hemodynamic status at presentation, laboratory parameters, management and outcome. The outcome was analyzed as recovery to discharge or death. DKA was diagnosed based on the following criteria: blood glucose >200mg/dl, ketonuria, and pH<7.3 or bicarbonate <15meq/dl. Renal failure was diagnosed based on the RIFLE criteria for renal failure and the worst score was taken as the final criteria. (4,5) The baseline creatinine value if not known, the value prior to discharge was taken as the baseline value or estimated creatinine clearance based on the height was used. All children were treated as per the existing hospital protocol for management for DKA. Children were treated based on the Milwaukee protocol in the year 2006 and from the year 2007 onwards they were treated as per the ISPAD protocol. (6,7) Strict intake output charts were maintained in all these children. Renal failure was managed conservatively and by peritoneal dialysis under the guidance of a pediatric nephrologist.

Results

Out of 130 children with DKA, 15 children (11.5%) had renal failure. The chronological age of the children at presentation ranged from 3 -12 years with a mean of 9.06 ± 2.68 years. Thirteen of the 15 (87%) children were diagnosed to have DKA at the emergency room, while the other two were diagnosed as acute CNS infection at admission. Male: female ratio was 1:2. New onset diabetes with DKA and renal failure was encountered in 8 episodes and 7 episodes occurred in known diabetic children. The diabetic age ranged from 1- 7 years.

Prehospital symptoms of ketoacidosis varied from 1 to 5 days. The mean prehospital illness duration among the survivors was 1.6 ± 0.9 days and 2.5 ± 1.5 days among non survivors. Initial fluid resuscitation required was 10- 60 ml/kg of normal saline at the emergency room. Out of the 15 children, 9 (60%) presented with shock of which 5 were hypotensive and 4 required inotropic support. On AVPU scale (alert, verbal, pain response, unresponsive) 4 were unresponsive, 8 were pain responsive and 3 were verbal responsive The mean blood glucose was 535 ± 122.4 mg/dl at presentation and ranged from 255 mg/dl - 718 mg/dl. Ten out of 15 (66.6%) children had increased renal parameters at presentation while five others had increasing parameters after hospitalization. pH on admission ranged from 6.8 - 7.28 with a mean of 6.94 ± 0.15. Initial bicarbonate at admission was 5.05 ± 3.21mg/dl. Ten of the 15 (66.6%) children had severe acidosis (ph<7.1). The duration of acidosis varied from 50 hours of hospitalization to 140 hours among those who survived. Serum osmolality ranged from 294 - 328mosm/l with a mean of 315 ± 8.7 mosm/l. pCO2 at admission was 15.4 ± 4.8 with a range of 8.5 - 22.

Infection work-up revealed sepsis in 5, urinary tract infection in 5, bronchopneumonia in 1, pyogenic meningitis in 2 and peritonitis in 1 child and E coli was grown in 4, klebsiella in 2 and pseudomonas in 2 children. One child had ARDS. Six of the known diabetic children had infection as a precipitating factor and 4 had poor compliance to insulin. Of the new cases, 4 had infection and 5 had shock. One child was diagnosed as rhabdomyolysis. Four (27%) children had anuria during the hospital stay and all of them died. The urine output in 14 children ranged from 0.8 ml/kg/hour to 5.6 ml/kg/hr in the first 12 hours of hospital stay. One child had presented with anuria. Four (27%) had features of fluid overload during therapy. The average fluid infused in the first 24 hours ranged from 1.5 times to 2 times the maintenance rate.

Study parameters of the 15 children are shown in table 1. The time interval between hospital admission and commencement of insulin infusion varied from 1 to 16 hours. The mean time interval among the survivors was 3 ± 2.3 hours and 5.7 ± 5.4 hours among non survivors. Of the electrolyte imbalance, 9 (60 %) had hypernatremia, 5 had hyperkalemia, and one had persistent hypokalemia. Abdominal ultrasonogram showed grade 1 to grade 3 renal parenchymal

Table 1: Study parameters in 15 children

	Age / gender	Fever	AVPU	Shock	Sugar (mg/dl)	Osmolality	Bicarbonate	Maximum urea mg/dl	Maximum Creatinine mg/dl	pH at admission	Pco2 at admission	Bicarbonate	Dialysis	Infection	Hypernatremia	Diabetic years	Glycemia	New/old Diabetic	Ventilator support	Survived
1.	3/F	Y	P	-	486	309	Y	98	1.6	6.97	10.2	2.3	-	Y	-	-	Y	N	-	Y
2.	8/F	Y	V	-	591	323	-	108	3.5	6.9	16.1	3.4	-	Y	Y	4	Y	O	-	Y
3.	11/F	-	P	-	524	321	Y	162	3.5	-	-	8	Y	Y	Y	-	Y	O	Y	-
4.	12/F	Y	P	Y	255	314	Y	222	4.5	6.9	15	6	Y	Y	Y	7	Y	O	Y	Y
5.	10/M	Y	P	Y	390	294	Y	143	4.3	6.89	15.1	2.7	Y	Y	-	-	Y	N	Y	-
6.	5/F	-	P	Y	490	319	-	101	2.0	-	-	10	-	-	Y	-	-	N	Y	Y
7.	8/M	Y	U	Y	586	319	Y	89	2.3	6.9	10	3.3	-	Y	Y	1	Y	O	Y	-
8.	12/F	-	P	Y	682	308	Y	135	3.6	6.9	15.7	3.3	-	-	-	-	Y	N	–	–
9.	7/F	Y	P	Y	540	316	Y	87	3.5	6.8	8.5	1.2	Y	-	-	-	-	N	Y	-
10.	12/F	-	V	Y	467	328	-	88	2.1	6.89	22	4.1		Y	Y	1	-	O	Y	Y
11.	11/M	Y	V	-	718	310	Y	111	6.4	7.28	21	10.3	Y	-	-	-	Y	N	-	Y
12.	8/M	Y	U	-	440	320	Y	117	2.0	7.19	20.3	7.6	-	Y	Y	7	Y	O	Y	-
13.	10/F	-	U	Y	700	323	Y	104	2.8	6.8	16.8	2.7	Y	-	Y	5	-	O	Y	-
14.	8/F	Y	U	-	573	320	Y	155	2.9	7.1	20.9	9.5	Y	Y	Y	1.7		O	-	Y
15.	11/M	-	P	Y	589	305	Y	70	2.2	6.81	9	1.4	-	Y	-	-	Y	N	-	Y

Y -Yes, M-Male, F-Female, P= Pain responsive, U = unresponsive., N -New, O- Old, ER - emergency room

disease, enlarged kidneys, hepatomegaly, bilateral hydronephrosis and free fluid abdomen. Seven children underwent peritoneal dialysis and the others were treated conservatively. But for the need of ventilatory support none of the factors like age, gender, shock, sensorium, initial glucose, bicarbonate, pH, pCO2, need for dialysis or presence of infections had statistically significant association with mortality in ARF. Features of cerebral edema were encountered in 6 children (40%) and 4 (66%) of them died. Multi organ dysfunction syndrome (MODS) was the cause of death in 3 children while one child had ARDS. Mortality in DKA with renal failure was 40%. Of the 9 children who survived, 7 were followed up after recovery and none of them had microalbuminuria and hence diabetic nephropathy was ruled out. Other two were lost for follow up.

Discussion

Pre renal azotemia is commonly encountered in DKA at the presentation and urea, creatinine becomes normal within few hours with adequate hydration. ARF is rare in DKA as the osmotic effect of hyperglycemia tends to preserve the intravascular volume with the associated diuresis. (1) Renal function during and after DKA could be divided into two groups: group A, where initially impaired renal function quickly returned to normal with correction of dehydration and this is commonly encountered in DKA; group B, where renal function continued to deteriorate for a variable period probably due to reversible renal ischemia. (2) Elevated blood urea, creatinine in DKA is not only due to prerenal azotemia due to volume depletion but also due to increased ureagenesis. Increased conversion of aminoacids to glucose produce hyperamminoacidemia and this increases the substrate availability for ureagenesis. (8) Pseudohypercreatinemia due to interference by acetones to create a spurious rise in creatinine (9) and ability to maintain normal urine output should not prevent one from diagnosing this complication in DKA especially in a child with persistent acidosis. Unusual elevation of creatinine alone, without increasing urea levels gives a clue for this laboratory error. The traditional alkaline picrate method (Jaffe method) gives values for serum creatinine that are 10 - 20% greater than those obtained using contemporary kinetic methods or any reference isotope dilution mass spectroscopy traceable method. (10) Out of the 15 children analyzed only one child had disproportionate rise of creatinine but this was explained by the release of preformed creatinine from the muscles in rhabdomyolysis. Persistent acidosis, increasing urea and creatinine despite adequate hydration with or without oliguria /anuria gave the clue for renal failure in the study group. Fourteen children had infection with ARF suggestive that infections in DKA can lead to renal failure.

In our patients, increasing urea, creatinine values, developing oliguria, anuria and failure of blood glucose to fall as expected despite adequate hydration, were commonly seen during the initial few hours of management. Persistent acidosis, altered sensorium and frequent hypoglycemic episodes during recovery were encountered in these children. However increasing urea creatinine may also indicate inadequate hydration leading to persistent acidosis hence the need to carefully monitor fluid therapy.

Insulin requirements are altered in renal failure, either increased due to insulin resistance or decreased due to impaired clearance of circulating insulin. Varied insulin sensitivity in these children makes them more

prone for frequent hypoglycemic episodes than children without renal failure and this necessitated using upto 12.5% dextrose containing intravenous fluids during therapy in our patients.

Management strategies for renal failure in DKA include restriction of fluids, using bicarbonate to combat acidosis (if pH <6.9), peritoneal dialysis/hemodialysis, adequate antibiotics to treat infection and prolonged insulin infusion at a lower dose (0.054mcg/kg/hour) with higher dextrose concentration in the intravenous fluids. Infections increase the mortality and morbidity in DKA and hence aggressive treatment is essential. Renal failure in DKA is rarely due to rhabdomyolysis and is treated by adequate alkalinization with bicarbonate and hemodialysis.

The study has its own limitations- it was a retrospective data analysis and the central venous pressure monitoring was not done in all children. The serum creatinine estimation was done using Jaffe method as the kinetic methods are not freely available. Over estimation of ARF due to this interference is unlikely as all the 130 children treated for DKA underwent the same method of estimation. Persistent acidosis with this setting was a valid clue for ARF. The reason for such high rates of ARF in the study could be explained by sepsis and delayed referral to the tertiary centre. This is a government run pediatric tertiary care centre that deals with the sickest of the sick children predominently from lower socioeconomic strata. The high incidence of hypovolemia and shock, severe acidosis and altered sensorium at presentation at the emergency room would indicate the delayed presentation in the study group.

Conclusion

Hypotensive shock and infections should be thought as etiological factors for acute renal failure in DKA. Renal failure though rare carries a high mortality in children with DKA.

References

1. Woodrow G, Brownjohn AM, Turney AH. Acute renal failure in patients with type 1 diabetes mellitus. Postgrad Med J. 1994; 70: 192-194
2. Muzulu S, Gregory R. Acute renal failure complicating diabetic ketoacidosis; an uncommon presentation of newly diagnosed IDDM. Practical Diabetes International. 1998; 5: 52-53
3. Al-matrafi J, Vethamuthu J, Feber J. Severe acute renal failure in a patient with diabetic ketoacidosis. Saudi J Kidney Dis Transpl. 2009; 20: 831-834
4. Eric AJ, Clermont G, Kersten A, Venkataraman R, Derek CA, Dirk DB, JohnAK. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. Critical Care. 2006; 10: R73
5. Rinaldo B, Claudio R, John AK, Ravindra M, Paul P and the ADQI Workgroup. Acute renal failure - definition, outcome measures, animal models, Fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group Critical Care. 2004; 8 :R204- R212
6. Ramin A, David T. Nelson Text book of Pediatrics. 17th edn. Elsevier, Philadelphia. 2004: 1958-1960
7. Wolfsdorf J, Craig ME, Daneman D, Dunger D, Edge J, Lee WR et al. ISPAD Clinical Practice Consensus Guidelines. 2006-2007. Diabetic ketoacidosis. Pediatr Diabetes. 2007; 8: 28-42
8. Irwin RS, Rippe JM. Irwin and Rippe's Intensive Care Medicine. 6thedn. Lippincott. Philadelphia. 2008; 1260 -1265
9. Nanji AA, Campbell DJ. Falsely-elevated serum creatinine values in diabetic ketoacidosis - clinical implications. Clin Biochem. 1981; 14: 91-93
10. Kevin VL. Estimating GFR in children: Schwartz redux. Nature reviews. Nephrology. 2009; 5: 310 -311

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